

# ROLE OF SOLUBLE GUANYLYL CYCLASE 11 (SGC11) ISOFORM IN MICE CORPUS CAVERNOSUM SMOOTH MUSCLE RELAXATION

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## **Aims:**

Soluble guanylyl cyclase (sGC) is, as major effectors molecule for NO, an interesting therapeutic target for the treatment of erectile dysfunction. Therefore, we assessed the functional importance of the predominant soluble guanylyl cyclase (sGC)  $\alpha_1\beta_1$  isoform in corpus cavernosum (CC) relaxation.

## **Methods:**

CC isolated from male  $sGC\alpha_1^{-/-}$  mice and wild type littermates were mounted in organ baths for measurement of agonist- or electrical field stimulation (EFS)-induced tension responses.

## **Results:**

The endothelium-dependent relaxation to acetylcholine (ACh) or bradykinin (BK) and the neurogenic response to electrical field stimulation (EFS) were nearly abolished in the  $sGC\alpha_1^{-/-}$  CC. The relaxing influence of exogenous NO (from sodium nitroprusside (SNP) and NO-gas) was also significantly decreased in the  $sGC\alpha_1^{-/-}$  mice. The remaining relaxation seen in the  $sGC\alpha_1^{-/-}$  mice with exogenous NO, was strongly but not completely inhibited by the sGC-inhibitor ODQ. In the preparations of the  $sGC\alpha_1^{-/-}$  mice, the response to BAY 41-2272 (NO-independent sGC-activator) and to T-1032 (phosphodiesterase type 5 inhibitor) were also significantly reduced. The specificity of the impairment of the sGC-related responses was demonstrated by the similar forskolin (adenylyl cyclase activator)-and 8 pCPT-cGMP (cGMP-analogue)-induced responses.

## **Conclusion:**

Our findings indicate the involvement of an sGC isoform with the  $\alpha$ -subunit in NO-induced CC smooth muscle relaxation. However, the remaining relaxing influence of exogenous NO in the  $sGC\alpha_1^{-/-}$  mice, suggests the contribution of (an) additional pathway(s).